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Emerging Treatment Approaches for EBC

Announcer:
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Dr. Gradishar:
Hello, I'm Dr. Bill Gradishar from Northwestern University. Welcome to CME on ReachMD. Today I'll review some of the emerging treatment options for early-stage breast cancer.

And as a sort of introduction, I think everybody recognizes that we've had a number of different strategies that we employ, either utilizing neoadjuvant therapy or adjuvant therapy or both, and we often make our decisions based on the features of the disease and the characteristics of the patient. So with that said, we can still think of breast cancer as being separated very broadly into hormone receptor-positive, triple-negative breast cancer, and HER2-positive breast cancer. And in each one of those lanes, there are emerging strategies to try and enhance the outcomes of patients.

Starting with the last first, we typically think of ER-positive breast cancer as one that is typically not all that chemotherapy-sensitive; we often rely on endocrine therapy alone, and immunotherapy has not found a footing in that space. But the KEYNOTE-756 trial, which reported recently, looked at the utilization of neoadjuvant chemotherapy with or without immunotherapy in the form of pembrolizumab for high-risk ER-positive patients. And it demonstrated that by utilizing pembrolizumab attached to the chemotherapy neoadjuvant regimen, you could significantly increase the PCR rate from about 15% to 24%.

Now that in and of itself shows a numerical advantage for the use of immunotherapy, but we of course have to determine whether or not we're going to see any critical endpoints improved as well. And specifically, I'm talking about event-free survival, which is a downstream clinical outcome, and then also overall survival. And in that experience, they found that patients with less strong ER expression or stronger PD-L1 status tended to have the greatest benefit from the addition of pembrolizumab.

We also know that antibody-drug conjugates have been a significant theme in a variety of different kinds of breast cancer over the last few years, both in the advanced-disease setting as well as early-stage setting. We've had an abundance of data emerging with trastuzumab deruxtecan, and that continues to be the case as we look for its use in earlier stages of disease. And a couple of examples of that include the DESTINY-B05 and DESTINY-B11 trial, the B standing for breast cancer.

And in the B05 trial, this is looking at the utilization of trastuzumab deruxtecan versus T-DM1 in patients who have residual disease following the administration of neoadjuvant therapy. The standard of care remains the use of T-DM1 in that setting, but we now have data in the metastatic setting suggesting T-DXd, or trastuzumab deruxtecan, may be a more effective therapy. So the DESTINY-Breast05 trial is evaluating that comparison to determine whether or not T-DXd, in fact, translates into better event-free survival and perhaps overall survival. We don't have data yet.

And the DESTINY-B11 trial, in contrast, is looking at whether or not introducing T-DXd in the neoadjuvant setting may offer some

advantage over the typical regimen, which is a taxane-trastuzumab-pertuzumab regimen. So in this trial, patients are either receiving trastuzumab deruxtecan for 4 cycles followed by a taxane-HP regimen, or dose-dense AC followed by trastuzumab and pertuzumab along with the taxane. So the B11 trial will look at PCR rates and then eventually, of course, look at the overall outcome of patients to determine if there is any advantage for this strategy.

Additionally, within the theme of antibody-drug conjugates, the drug datopotamab deruxtecan is another agent that has significant activity in metastatic disease, and it's being evaluated in an earlier-stage setting as well. So in the TROPION-Breast03 trial, there is an effort to determine in patients with triple-negative breast cancer who receive neoadjuvant therapy and then at the time of surgery are found to have residual disease. They will be randomized to datopotamab deruxtecan, or Dato-DXd as a shorthand, along with durvalumab, an immunotherapy. And the comparison will be to capecitabine-pembrolizumab or to Dato-DXd. So, again, this is a trial ongoing; we don't have the data from this trial. But again, it's an effort to see if we can improve outcomes of patients who are deemed to be at continued high risk of disease recurrence because of residual disease that is identified at the time of surgery. So this is a trial that builds on observations made in the metastatic disease setting, showing that Dato-DXd has significant activity, might it translate into improving outcomes in those patients with earlier stages of the disease.

Now, all of these trials are likely to show some differences in early events such as PCR rates, but the ultimate measure of the efficacy will be in whether or not event-free survival and overall survival are improved. And also, even if those measures are improved, at what cost do they come with respect to side effects? So all of those elements need to go into consideration when thinking about how these therapies may displace what we currently think of as first-line therapy. And ultimately, these may influence guidelines, such as the NCCN Guidelines, and if and when and how we incorporate these into standard therapies that are available to patients.

Thank you for your attention. I hope this discussion was useful in your practice.

Announcer:
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